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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,124	07/18/2003	Martin F. Bachmann	1700.0340001/BJD/KMH	3313

26111 7590 06/29/2010

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EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
06/29/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,124	BACHMANN ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63, 68-76, 78-88, 94, 97-116, 118-123, 126, 128-139* is/are pending in the application.

4a) Of the above claim(s) *74,99,105-107,111-113,121-123 and 133* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims rejected are 63,68-73,75,76,78-88,94,97,98,100-104,108-110,114-116,118-120,124,126,128-132 and 134-139.

DETAILED ACTION

The Amendment filed April 15, 2010 in response to the Office Action of October 15, 2010 is acknowledged and has been entered. Claims 74, 99, 105-107, 111-113, 121-123 and 133 are withdrawn. Claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are under consideration in this Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stockley et al. (US Patent 6,159,728) in view of Deghengi et al. (US 2002/0187938), Kojima et al. (Nature, 1999 Vol. 402, p. 656-660) Maita et al. (Gen Pept Accession VCBPQB, 1971) and further in view of Nielsen et al. (US Patent 6,548,651 B1) **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicants argue that the compositions of the present invention are able to induce high levels of antibodies that surprisingly recognize the n-octanoylated form of ghrelin as shown in the present specification, in particular in Example 17. Applicants argue that the generated antibodies also recognized the alternative isorform, Ghrelin-desQ14 and as a result, antibodies generated from vaccination with

C- or N- terminally linked ghrelin and ghrelin peptide, to a core particle or, preferably to a VLP, were able to block the entry of n-octanoylated ghrelin into the brain and modulated food intake in mice.

In response to Applicant's arguments the Examiner notes that Applicant has not provided any scientific reasoning for why the generation of high levels of antibodies against the n-octanoylated form of ghrelin would have been unexpected. Applicant has not provided any scientific reasoning or evidence for why it would have been unexpected that the antibodies against the ghrelin peptide would modulate the food intake in mice. It is the Examiner's position that the skilled artisan would have expected that immunization of animals with the VLPs conjugated to ghrelin peptide would generate ghrelin peptide specific antibodies which would block the ghrelin peptide from stimulating the growth hormone which would result in the modulation of the food intake. This is because it has been known in the prior art that immunization with ghrelin peptides induced ghrelin specific antibodies (as evidenced by Nakazato et al., the reference of record in the Office action on 1/12/2006) and because Stocley teaches using VLP of an RNA pacteriophage as an antigen delivery system (see claims 1-12) and because Deghengi teaches that administration of ghrelin peptide antagonists in rats results in decreased level of circulating growth hormone (see Example 1). Thus the unexpected results argued by Applicant would have been expected by the skilled artisan at the time of the present invention and therefore the rejection is maintained.

Applicant argues that the references cited by the Examiner, viewed alone or in combination, neither disclose nor suggest all of the elements of the present claims in their proper association and function, with any degree of predictability and expectation of success. Applicants

argue that the cited references do not disclose or suggest a composition comprising a virus-like particle with at least one first attachment site wherein said first attachment site is a lysine residue of said virus-like particle and said second attachment site is a cysteine residue, as recited in the present claims. Applicants argue that Stockley does not disclose the association of non-peptide covalent bonds of lysine residues of virus-like particles of an RNA-bacteriophage as first attachment sites with cysteine residues of the ghrelin antigens as second attachment sites forming highly ordered and repetitive ghrelin arrays representing for the induction of immune responses against ghrelin. Applicant argues that there is nothing in Stockley, Nielsen or any of the other cited references that would have led one of ordinary skill in the art to have used a lysine residue of a virus-like particle of an RNA-bacteriophage as a first attachment site, and to bind such a residue via a non-peptide covalent bond to a cysteine residue of ghrelin or a ghrelin peptide as a second attachment site, thereby forming a highly ordered and repetitive ghrelin array useful for the induction of immune responses against ghrelin. Applicant argues that Examiner has not provided sound scientific reasoning to support the assumption, that making a change to the disclosure of Stockley would have yielded predictable results and Examiner has not provided a sound reason for why the skilled artisan would make the modification of Stockley.

In response to Applicant's arguments the Examiner notes that the lysine residue of the first attachment site in the VLP and the cysteine residue on the second attachment site on the antigen are amino acids binding the linker which connects the VLP to the antigen (specification [0050-0051]).

[0050] Attachment Site, First: As used herein, the phrase "first attachment site" refers to an element of non-natural or natural origin, to which the second attachment site located on the antigen or antigenic determinant may associate. The first attachment site may be a protein, a polypeptide, an amino acid, a peptide, a sugar, a polynucleotide, a natural or synthetic polymer, a

secondary metabolite or compound (biotin, fluorescein, retinol, digoxigenin, metal ions, phenylmethylsulfonylfluori- de), or a combination thereof, or a chemically reactive group thereof. The first attachment site is located, typically and preferably on the surface, of the core particle such as, preferably the virus-like particle. Multiple first attachment sites are present on the surface of the core and virus-like particle, respectively, typically in a repetitive configuration.

[0051] Attachment Site, Second: As used herein, the phrase "second attachment site" refers to an element associated with the antigen or antigenic determinant to which the first attachment site located on the surface of the core particle and virus-like particle, respectively, may associate. The second attachment site of the antigen or antigenic determinant may be a protein, a polypeptide, a peptide, a sugar, a polynucleotide, a natural or synthetic polymer, a secondary metabolite or compound (biotin, fluorescein, retinol, digoxigenin, metal ions, phenylmethylsulfonylfluoride), or a combination thereof, or a chemically reactive group thereof. At least one second attachment site is present on the antigen or antigenic determinant. The term "antigen or antigenic determinant with at least one second attachment site" refers, therefore, to an antigen or antigenic construct comprising at least the antigen or antigenic determinant and the second attachment site. However, in particular for a second attachment site, which is of non-natural origin, i.e. not naturally occurring within the antigen or antigenic determinant, these antigen or antigenic constructs comprise an "amino acid linker".

Contrary to Applicant's assertions the lysine and the cysteine attachment sites as well as the non-peptide covalent bond linker are expressly taught in Nilsen. Nielsen teaches a non-peptide heterobifunctional cross-linker succinimidyl 6-(β-maleimido-propionamido) hexanoate (SMPH) covalently linking peptides with nucleic acid molecules representing bacterial antigens through either a cysteine (C) or a lysine (K) residue (see claim 1, Tables 1, 4, and 8, column 8, lines 17-41 and column 9, lines 4-10).

It would have been *prima facie* obvious to the person of ordinary skill in the art to covalently attach Stockley's RNA Qβ bacteriophage to Deghenghi's and/or Kojima's ghrelin peptide using Nielsen's non-peptide heterobifunctional cross-linker succinimidyl 6-(β-maleimido-propionamido) hexanoate (SMPH) bound to the first attachment site which is a lysine present on the VLP and a second attachment site which is a cysteine present on the antigen because Nielsen teaches that the cysteine and lysine residues are the amino acids that are

successfully used to connect nucleic acids molecules with antigens via non-peptide SMPH linker (see claim 1, Tables 1 and 4, column 8, lines 17-41 and column 9, lines 4-10).

It is the Examiner's position that the skilled artisan would have had a reasonable expectation of success to covalently attach Stockley's RNA Qβ bacteriophage to Deghenghi's and/or Kojima's ghrelin peptide using Nielsen's non-peptide heterobifunctional cross-linker succinimidyl 6-(β-maleimido-propionamido) hexanoate (SMPH) bound to the first attachment site which is a lysine present on the VLP and a second attachment site which is a cysteine present on the antigen because Nielsen teaches that the cysteine and lysine residues are the amino acids that are successfully used to connect nucleic acids molecules with antigens via non-peptide linker.

Thus in view of the foregoing the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Rejection of Claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 11/663,350 **is maintained.**

Rejection of Claims 63, 68-73, 75, 76, 78-88, 94, 97, 98, 100-104, 108-110, 114-116, 118-120, 124, 126, 128-132 and 134-139 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 4, 8, 13-23, 25 and 36-51 of copending Application No. 11/664,716 **is maintained.**

Applicant requests that the rejection is held in abeyance until allowable subject matter is indicated.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648